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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/790,043	01/28/1997	DAVID PAYNE	GM50005	9942
25181	7590	06/25/2004	EXAMINER	
FOLEY HOAG, LLP PATENT GROUP, WORLD TRADE CENTER WEST 155 SEAPORT BLVD BOSTON, MA 02110			PRIEBE, SCOTT DAVID	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 06/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

9M

Office Action Summary

Application No.

08/790,043

Applicant(s)

PAYNE ET AL.

Examiner

Scott D. Priebe

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 61-67 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 61-67 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

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DETAILED ACTION

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Provisional application 60/024,845 does not disclose instant SEQ ID NO: 1 and SEQ ID NO: 2, to which the instant claims are directed. The nucleotide sequence disclosed in the '845 application comprises a sequence, nucleotides 281-1050, that are similar but not identical to instant SEQ ID NO: 1. The nucleotides 1041-1050 of the sequence in the '845 application are CAATTAATAN, whereas the last 11 nucleotides of instant SEQ ID NO: 1 are CAATTAAATAAA. The amino acid sequence disclosed in the '845 application appears to comprise the amino acids 1-255 of instant SEQ ID NO: 2, but does not comprise the C-terminal Lys residue (a.a. 256) of instant SEQ ID NO: 2, and instead comprises Asn at amino acid 256 followed by 36 additional amino acids. Consequently, the effective filing date of the instant application is its actual filing date of 1/28/97, not that of the '845 application.

Claim Rejections - 35 USC § 112

Claims 61-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid sequence comprising a nucleotide sequence that encodes a polypeptide that reduces crotonyl-CoA or crotonyl-ACP and comprises an amino acid sequence either identical to SEQ ID NO: 2, or differing from SEQ ID NO: 2 by substitution, insertion or deletion of a single amino acid, does not reasonably provide enablement for a nucleotide sequence encoding a polypeptide that reduces crotonyl-CoA or crotonyl-ACP and differs from SEQ ID NO: 2 by insertion, deletion or substitution more than one amino acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

This rejection pertains to parts (d) and (e) of claim 61, part (g) of claim 61 as it relates to parts (d) and (e), and claims 62-67 as directed to this subject matter. These embodiments are directed to an isolated nucleic acid that encodes a polypeptide that reduces crotonyl-CoA or crotonyl-ACP and has an amino acid sequence that is identical to SEQ ID NO: 2 or that may differ from SEQ ID NO: 2 by substitution, insertion or deletion of up to 12-13 amino acids (part (d)) or by conservative substitution of up to 10 amino acids.

It is well known in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure is neither well understood nor predictable (see Ngo, pp. 433 and 492-495). The number of possible amino acid sequences that are of a given % identity relative to a reference sequence,

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where all differences between the possible sequences and the reference sequence are substitutions, can be calculated by the following formula:

$$N = XL + X^2L(L-1)/2! + X^3L(L-1)(L-2)/3! + \dots + X^{n-1}L(L-1)(L-2)\dots(L-(n-2))/(n-1)! + X^nL(L-1)(L-2)\dots(L-(n-1))/n!$$

where N is the number of possible sequences, X is the number of different residues that can be substituted for a residue in the reference sequence, L is the length of the reference sequence, n is the maximum number of residues that can be inserted, deleted or substituted relative to the reference sequence at a given % identity. The last term of the expansion is far larger than the penultimate term, and provides a close approximation of the sum. The last term of the expansion is equal to $X^nL/(L-n)!n!$. For an amino acid sequence, X is 19 (alternate amino acids). For SEQ ID NO: 2, L is 256 (amino acids). When n=12, as permitted by claim 61, part(d), N is approximately equal to 3×10^{35} or 300,000,000,000,000,000,000,000,000,000 amino acid sequences that differ from SEQ ID NO: 2 by up to 12 amino acid substitutions. For n=11, N would be 7×10^{32} possible amino acid sequences. These calculations do not include a greater number of amino acid sequences that differ from SEQ ID NO: 2 by amino acid deletions or insertions or a mixture of deletions, insertions and substitutions of up to 12 amino acids, as permitted by claim 61, part (e).

The specification contains no guidance or citations of relevant prior art that would inform the skilled artisan of which amino acid residues of SEQ ID NO: 2 could be altered without adversely affecting its folding or its biological activity. The specification discloses a single species of polypeptide readable on the claims that reduces crotonyl-CoA or crotonyl-ACP, and that is a naturally occurring polypeptide. The specification does not disclose a single working

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example of a functional polypeptide readable on the claims that is artificial, i.e. whose sequence was determined by man rather than by nature. To determine which of the high number of sequences possible amino acid sequences (differing by up to 12 amino acids) encompassed by the claims that would encode a polypeptide that reduces crotonyl-CoA or crotonyl-ACP would require excessive trial and error experimentation. As set forth in *In re Fisher*, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

In *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991), the court ruled that a claim to a large genus of possible genetic sequences encoding a protein with a particular function that needs to be determined subsequent to the construction of the genetic sequences may not find sufficient support under 35 USC 112, 1st para., if only a few of the sequences that meet the functional limitations of the claim are disclosed and if undue experimentation would be required of one skilled in the art for determining other genetic sequences embraced by the claim. This is the case here, where specification discloses only a single naturally-occurring amino acid sequence and nucleotide sequence having the necessary properties for the disclosed use. In light of the limited guidance for making polynucleotides having the necessary properties and the failure of state of the prior art to provide the information missing from the specification, the limited number of working examples, the unpredictable nature of determining the useful sequences *a priori*, the excessive trial and error experimentation

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that would then be required to identify the useful sequences within the claimed groups of polynucleotides, it would require undue experimentation to make and use the polynucleotides commensurate in scope with the claimed invention for the uses disclosed in the specification.

Claim Rejections - 35 USC § 102

Claims 61-67 are rejected under 35 U.S.C. 102(e) as being anticipated by Kunsch et al. US 6,593,114, which claims priority through US application 08/781,986, filed 1/3/97.

Kunsch et al. discloses a polynucleotide comprising SEQ ID NO: 772. (This sequence is also disclosed as SEQ ID NO: 772 in the '986 application.) Nucleotides 24-704 of SEQ ID NO: 772 corresponds to nucleotides 1-678 of instant SEQ ID NO: 1. Col. 103-104 indicates that SEQ ID NO: 772 contains an open reading frame from nucleotides 1-677, which corresponds to nucleotides 1-652 of instant SEQ ID NO: 1. Over this region, SEQ ID NO: 772 differs from instant SEQ ID NO: 1 by four mispairs (at nucleotides 93, 468, 540, 571 of instant SEQ ID NO: 1) and two insertions of a single nucleotide (between nucleotides 627 and 628 and between nucleotides 650 and 651 of instant SEQ ID NO: 1). The first mispair is an A or C vs. A in SEQ ID NO: 1. This mispair occurs in the codon for amino acid 31 of instant SEQ ID NO: 2, and would encode either the same amino acid or a different amino acid as in SEQ ID NO: 2. The second and third mispairs do not change the amino acid encoded by SEQ ID NO: 2. The fourth mispair would result in coding for a different amino acid (amino acid 191 of SEQ ID NO: 2). The insertions cause a shift in reading frame after the codon for amino acid 209 of SEQ ID NO: 2. Consequently, SEQ ID NO: 772 would encode amino acids 1-190 and 192-209, or 1-30, 32-190, and 192-209 of SEQ ID NO: 2, depending on the choice of A or C, respectively, at the first

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mispair. Kunsch also discloses expression vectors comprising SEQ ID NO: 772, and host cells, such as bacterial or mammalian cells, comprising the vectors (col. 5-6, 15-19, for example).

The polynucleotide comprising SEQ ID NO: 772, vector and cells disclosed by Kunsch anticipate the instant claims as they relate to part (c) of claim 61. The near identity of the prior art sequence to the corresponding region of instant SEQ ID NO: 1 shows that the prior art sequence would hybridize to under "stringent conditions" as they are defined in the instant specification (at least 95% identity over the paired region). It is noted that for the nucleotide sequence to hybridize to SEQ ID NO: 1, it need not be complementary over the entire length of SEQ ID NO: 1.

Applicant's arguments filed 4/12/04 have been fully considered but they are not persuasive. The Examiner agrees that it is not clear provisional application 60/009,861 supports the disclosure of SEQ ID NO: 772 in the '114 patent. However, the '986 application (filed 1/3/97) discloses a SEQ ID NO: 772 identical to SEQ ID NO: 772 of the patent. As indicated above, instant SEQ ID NOs: 1 and 2 are not supported by the disclosure of the '845 application. As a result, the '114 is prior art under 35 U.S.C. 102(e).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

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provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 61-67 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,432,670. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims embrace the subject matter claimed in the patent.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

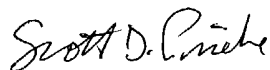
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (571) 272-0733. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy J. Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Scott D. Priebe
Primary Examiner
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